

CLAIMS

1. A modified functional modular polyketide synthase (PKS) system, or a functional portion thereof, said functional portion comprising at least two modules, of said PKS, wherein said PKS has been modified to prevent its utilization of its native starter unit, but wherein said PKS is able to incorporate a diketide substrate into a polyketide that is at least a triketide.
2. The PKS of claim 1, which is contained in a host cell.
3. The PKS of claim 2, wherein the host cell is heterologous to said modified PKS.
4. The PKS of claim 2, wherein the host cell is a *Streptomyces* host cell.
5. The PKS of claim 2, wherein the host cell is permeable to the diketide substrate.
6. The PKS of claim 2, wherein the host cell has been modified to delete a native PKS contained in said cell.
7. The PKS of claim 6, wherein the host cell is *S. coelicolor* CH999.
8. The PKS of claim 1, wherein the diketide substrate is that obtained by the coupling of a starter unit which is acetyl CoA, malonamyl Co-A, propionyl Co-A, butyryl Co-A, isobutyryl Co-A, isovaleryl Co-A, benzoyl Co-A, aminobenzoyl Co-A, aminohydroxybenzoyl Co-A, or thiophene carboxyl Co-A, with an extender unit which is malonyl Co-A, methylmalonyl Co-A or ethylmalonyl Co-A.
9. The PKS of claim 2, wherein the diketide substrate is that obtained by the coupling of a starter unit which is acetyl CoA, malonamyl Co-A, propionyl Co-A, butyryl Co-A, isobutyryl Co-A, isovaleryl Co-A, benzoyl Co-A, aminobenzoyl Co-A, aminohydroxybenzoyl Co-A, or thiophene carboxyl Co-A, with an extender unit which is malonyl Co-A, methylmalonyl Co-A or ethylmalonyl Co-A.

10. The PKS of claim 1, wherein the diketide substrate is in the form of an N-acetyl cysteamine (NAC) thioester.

11. The PKS of claim 10, wherein the diketide substrate is (2S,3R)-2-methyl-3-hydroxypentanoyl-NAC thioester.

12. A method to produce a desired polyketide, which method comprises:

(a) providing a modified functional modular polyketide synthase (PKS) system, or a functional portion thereof, said functional portion comprising at least two modules of said PKS, wherein said PKS has been modified to prevent its utilization of its native starter unit, but wherein said PKS is able to incorporate a diketide substrate into a polyketide that is at least a triketide;

(b) adding to said PKS a diketide substrate for said PKS;

(c) incubating said PKS and said diketide substrate under conditions wherein said polyketide is synthesized; and

(d) optionally recovering said polyketide.

13. The method of claim 12, wherein said PKS is contained in a host cell.

14. The method of claim 13, wherein the host cell is heterologous to said PKS.

15. The method of claim 13, wherein the host cell is a *Streptomyces* host cell.

16. The method of claim 13, wherein the host cell is permeable to said diketide substrate.

17. The method of claim 13, wherein the host cell has been modified to delete a native PKS contained in said cell.

18. The method of claim 17, wherein the host cell is *S. coelicolor* CH999.

19. The method of claim 12, wherein the diketide substrate is that obtained by the coupling of a starter unit which is acetyl CoA, malonamyl Co-A, propionyl Co-A, butyryl Co-A, isobutyryl Co-A, isovaleryl Co-A, benzoyl Co-A, aminobenzoyl Co-A, aminohydroxybenzoyl Co-A, or thiophene carboxyl Co-A, with an extender unit which is malonyl Co-A, methylmalonyl Co-A or ethylmalonyl Co-A.

20. The method of claim 13, wherein the diketide substrate is that obtained by the coupling of a starter unit which is acetyl CoA, malonamyl Co-A, propionyl Co-A, butyryl Co-A, isobutyryl Co-A, isovaleryl Co-A, benzoyl Co-A, aminobenzoyl Co-A, aminohydroxybenzoyl Co-A, or thiophene carboxyl Co-A, with an extender unit which is malonyl Co-A, methylmalonyl Co-A or ethylmalonyl Co-A.

21. The method of claim 12, wherein the diketide substrate is in the form of an N-acetyl cysteamine (NAc) thioester.

22. The method of claim 21, wherein the diketide substrate is (2S,3R)-2-methyl-3-hydroxypentanoyl-NAc thioester.